REMARKS / ARGUMENTS

Applicants' undersigned attorney wishes to express her appreciation to the Examiner for the courtesy of the telephone interview conducted to discuss the outstanding Office Action.

Upon entry of this amendment, the claims pending are claims 1, 2, 4-20, 22, 25, 26, 29-32, 37, 38, and 41-50.

Applicants acknowledge with appreciation the examiner's finding that claims 22, 25, 26, 29-32, 37, 38, 45-47 and 29 appear free of the art and otherwise allowable.

Claims 3, 21, 23, 24, 27, 28, 33-36, 39 and 40 were cancelled by previous amendments. These claims stand canceled without prejudice to refiling in a continuation application. Applicants further affirm the correctness of the inventive entity in view of the cancellation of the non-elected claims.

Claim 1 has been amended to incorporate the term "human" before both occurrences of PTP1B. Claims 29, 37, 38, 41, 45, 47 and 49 have been amended to incorporate the subject matter of claim 1, thus avoiding dependencies on presently rejected claim 1. Claim 14 is amended to change "modulates" to "decreases". Claim 41 is amended to delete the phrase "preventing or". Claim 50 is new and is supported in the specification at pages 90, line 10 through page 93, line 6. No new matter was added by these amendments, which are supported in the original specification. Any subject matter canceled from the claims by amendment is reserved for refiling in a continuation application filed during the pendency of this application.

Rejections Under 35 USC §112, first paragraph

Claims 14 and 41-44 are rejected under the first paragraph of §112 for lack of enablement of the scope claimed.

Claim 14 is rejected because no evidence has been provided for the ability to *increase* expression of target gene expression following administration of antisense.

Specifically with regard to claims 41-44, the examiner states that the ability to reduce blood glucose levels or delay onset of increasing glucose levels is not representative of the ability to prevent for an undefined timespan an increase in any and all glucose levels in any animal following administration of antisense of these claims.

Applicants respectfully request reconsideration and withdrawal of this rejection in view of the above amendments to the claims and the following remarks.

The amendment of Claim 14 changing "modulates" to "decreases" removes this ground of rejection therefrom. Similarly, the amendment of Claim 41, deleting the phrase "preventing or" should also satisfy this ground of rejection as against claims 41-44. Applicants reserve the subject matter thus canceled from the claims for refiling in a continuation application.

This basis for rejection may be properly withdrawn in view of the amendments.

Claim Rejections based on 35 USC §103(a)

All composition claims 1, 2, and 4-14 and all *in vitro* method claims 15-20 and 48 are rejected as obvious in view of Huang *et al* 1998 *FASEB J.*, *12*(4):A188, Abstract 1099 (Huang), US Patent No. 5,726,027 (Olefsky) and Chernoff *et al*, 1990, *PNAS, USA*, *87*:2735-2739 (Chernoff), further in view of Milner *et al*, 1997 *Nature*, *15*:537-541 (Milner) and US Patent No. 5,801,154 (Baracchini).

Applicants respectfully request reconsideration and withdrawal of this rejection in view of the following remarks.

Huang is an abstract that mentions use of a single **unidentified** 15-mer oligonucleotide against PTP1B to knockout the activity of PTP1B in ***rat*** cells in culture. Huang discloses no information about the sequence of this oligonucleotide. In fact, Huang fails to identify whether its unidentified oligomer is complementary to **rat** PTP1B or human PTP1B. Because Huang does identify the oligonucleotide sequence, it does not permit identification of ***human*** PTP1B sequence, SEQ ID NO: 243, as the target. The lack of identification of the oligonucleotide by Huang also makes it impossible to determine what level of inhibition would be provided, if any, much less the 50% inhibition, as required by claim 50.

Huang may actually refer to an antisense sequence that specifically hybridizes with and/or binds **rat** PTP1B only. Given the inadequate information in Huang, one of skill in the art cannot determine whether Huang's unidentified oligonucleotide would bind **human** PTP1B. One of skill in the art cannot determine if Huang's unidentified oligonucleotide would **inhibit** human PTP1B. Both these characteristics of the oligonucleotides vis-à-vis human PTP1B are **requirements** of claim 1 and necessary for the practice of claim 15, and their dependent claims.

Olefsky refers to antisense technology as a tool and states that **again unidentified** antisense sequences to human PTP1B in general would be useful for inhibiting expression of PTP1B DNA or RNA. Olefsky does not provide any such oligonucleotides, nor does Olefsky teach or suggest the target regions of the PTP1B gene at all, much less SEQ ID NO: 243.

Thus Olefsky cannot teach antisense sequences that bind to SEQ ID NO: 243 as recited by claim 1 and as used in the method claims 15-20 and 48. Thus, Olefsky suffers from the same defects in disclosure as does Huang. The combination of these disclosures does not suggest in any way oligonucleotides that are capable of inhibiting **human** PTP1B of SEQ ID NO: 243 at any specific level of inhibition, much less the 50% inhibition required by claim 50.

Chernoff's disclosure of the cloning of a PTP1B contains no suggestion of antisense compounds targeted to ***any*** region of the PTP1B gene. Chernoff does not teach or suggest any specific sequences for antisense compounds that bind to SEQ ID NO: 243, and inhibit expression of PTP1B, as required by claim 1 and the methods using the sequences of claim 1. Chernoff's teachings, when added to the essentially duplicate disclosures of Olefsky and Huang, do **not** suggest in any way oligonucleotides that are capable of inhibiting human PTP1B at any specific level of inhibition, much less the 50% inhibition required by claim 50. Thus, Chernoff does not add anything to the primary references taken with the other secondary references that would make obvious the invention of the pending claims.

Milner's description of a generic screening technique similarly provides no suggestion that permits one to identify or suggest SEQ ID NO: 243 as a target PTP1B sequence for binding by the antisense sequences. Milner does not teach or suggest any specific sequences for antisense compounds capable of inhibiting expression of SEQ ID NO: 243, as required by claim 1 and the methods of claim 15. Further, Milner's generic teachings added to Chernoff's teachings, Olefsky's suggestions of unidentified antisense sequences, and Huang's unidentified oligonucleotide do **not** suggest in any way oligonucleotides

that are capable of inhibiting human PTP1B at any specific level of inhibition, much less the 50% inhibition required by claim 50. Thus, Milner does not add anything to the primary references taken with the other secondary references that would make obvious the invention of the pending claims.

Baracchini refers to modifications of antisense oligonucleotides in general, and specifically refers to multidrug resistance-associated protein (MRP), *not PTP1B*. Baracchini thus contains no disclosure that in any way suggests or refers to the compositions and methods of the present invention. Baracchini similarly provides no suggestion that permits one to identify or suggest SEQ ID NO: 243 as a target PTP1B sequence for binding by the antisense sequences. Baracchini does not teach or suggest any sequences for antisense compounds that bind to SEQ ID NO: 243, as required by claim 1 and the methods using the sequences of claim 1. Further, Baracchini's generic comments, added to the teachings of Milner, Chernoff, Olefsky and Huang do not suggest in any way oligonucleotides that are capable of inhibiting human PTP1B at any specific level of inhibition, much less the 50% inhibition required by claim 50. Thus, Baracchini does not add anything to the primary references taken with the other secondary references that would make obvious the compositions and *in vitro* methods of claims 1, 2, 4-20, 48 and 50.

In view of the claim amendments and these remarks, Applicants submit that this rejection should be properly withdrawn as against the pending claims.

In view of the above amendments and remarks, Applicants respectfully submit that the claim rejections have been overcome and that the present application is in condition for

allowance. Accordingly, allowance of the present application is respectfully requested.

Please charge any deficiency or credit any overpayment for entering this Amendment to our deposit account no. 08-3040.

Respectfully submitted,

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